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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,259	02/22/2005	Margaret Sin Ka Wan	13404US	5000

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,259	WAN, MARGARET SIN KA	
	Examiner	Art Unit	
	SUSAN E. FERNANDEZ	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-20,22,24-30,35,36 and 49-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18-20,22,24-30,35,36 and 49-53* is/are rejected.

7)☒ Claim(s) *4,16,19,50 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 29, 2009, has been received and entered.

Claims 17, 21, 23, 31-34, and 37-48 are cancelled.

It is noted that two claims are labeled as claim 35. The second of these claims was formerly labeled as claim 36 in the previous amendment. The second claim 35 will be treated as claim 36. In future amendments, applicant must fix the numbering of the claims in compliance with Rule 1.121.

Claims 1-16, 18-20, 22, 24-30, 35, 36, and 49-53 are pending and examined on the merits to the extent they read on the elected subject matter.

Claim Objections

Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 4 repeats that the cell diameter is from 5 to 10 times greater than the fibre diameter, which is recited in parent claim 1 at lines 9 and 10.

Claims 16, 19, 50, and 51 are objected to because of the following informalities: Claim 16 recites at line 8 "fiber" which should be replaced with "fibre" for consistency. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 comprises new matter as it specifies that the gaps between adjacent fibre portions are in the range of from about 2.0 μm to about 500 μm, whereas the disclosure teaches that the gap size is in the range from about 10 to 500 microns (page 11, lines 17-18) or from about 25 to 3000 microns (page 11, line 20). The lower limit of the gap size in claim 14 is not taught by the disclosure.

Claim 22 comprises new matter as it specifies a polymer solution emulsion or suspension whereas the disclosure does not have any recitation of the terms of "emulsion" and "suspension."

Because the specification as filed fails to provide clear support for the new claim language, a new matter rejection is clearly proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15, 18, 20, 22, 27-30, 35, 36, 49, and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 18, and 20 are indefinite because the recitation "said biologically compatible polymer liquid" lacks antecedent basis. Thus, claims 1-13, 15, 18, 20, 22, 27-30, 35, 36, 49, and 53 are rejected under 35 U.S.C. 112, second paragraph.

Claim 3 is indefinite because the range of 1 to 20 times the fibre diameter does not further limit the range recited in claim 1 of 5 to 10 times the fibre diameter. The range in claim 3 is broader than the range of parent claim 1.

Claim 10 is indefinite because the term "polylactide" on line three is followed by a period but is then followed by another sentence.

Claim 14 is indefinite because the recitation at lines 8 and 9 of "…adjacent fibre portions said gaps being…" is improper grammar. It appears that a comma should follow the term "portions." Furthermore, the claim is indefinite since the last term "scaffold" is followed by both a comma and then a period. The comma should be deleted.

Claim 18 is indefinite since the recitation "applying the cells to the fibre scaffold without addition of extrinsic biological factor wherein after a period of time, in the resulting cells having a morphology resembling nerve cells" is confusing. It appears that after a period of time, the resulting cells have a morphology resembling nerve cells.

Claim 22 is indefinite because the term "solution" is followed by a period but them is followed by another sentence.

**modify below for new claim limitations

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16, 18, 20, 22, 24-28, 35, 36 (the second claim labeled as claim 35), and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shastri et al. (WO 97/16545) in view of Coffee et al. (WO 98/03267), Sussman et al. (US 5,266,476), and Leong et al. (US 5,686,091).

Shastri et al. discloses a method for altering the regeneration, differentiation, or function of cells (claim 1), wherein cells are attached to a surface comprising an electrically conducting polymer (such as a biocompatible polymer, see claim 10). See also the abstract which indicates that conductive polymers are seeded with nerve cells. As indicated at page 15, lines 13-19, the electrically conducting polymer should be porous, where the pores should allow for vascular ingrowth and the seeding of cells without damage to the cells or patient, said pores generally in the range of between approximately 100 and 300 microns. Further still, the Shastri invention can be used to alter the regeneration, differentiation, or function of cells including various "organ cells", muscles cells, and "cells forming bone and cartilage" (page 18, lines 24-27).

Shastri et al. differs from the claimed reference in that it does not expressly disclose that the polymer on which the cells are attached is a fibre scaffold created by supplying a liquid comprising the biologically compatible polymer to a liquid outlet in the vicinity of a surface and

subjecting the liquid issuing from the outlet to an electric field to cause the liquid to form polymer fibre which is attracted to and deposits onto the surface.

Coffee et al. discloses a method of depositing fibres on a surface wherein a liquid comprising a biocompatible polymer is subjected to an electrohydrodynamic process in the vicinity of said surface (page 4, third paragraph). See Figure 1. Thus, Coffee et al. discloses supplying liquid comprising compatible polymer to a liquid outlet in the vicinity of a surface and subjecting liquid issuing from the outlet to an electric field to cause the liquid to form polymer fibres which are attracted to and deposit onto the surface to form a polymer fibre scaffold, as required by certain limitations in parent claims 1, 14, 16, 18, 20, and 24. Given that the Coffee method can be used to form a mat or web of fibres (page 21, last paragraph, and Figure 9), Coffee et al. teaches the creation of a three-dimensional continuous network of intercommunicating fibre portions.

Additionally, Coffee et al. teaches that the fibres can have a diameter in the range of 10 nm to above 100 microns (page 17, first paragraph, second to last sentence), which meets the diameter limitation of instant claims 1, 5-7, 13-16, 18, 20, and 24. Further still, the reference teaches that the liquid comprising a biocompatible polymer can be a solution or a melt (page 22, last paragraph) and the polymer can be polylactic acid (polylactide) (page 4, second paragraph) or "New Skin" wherein the fibres formed are approximately 0.5 to 5 microns in diameter (page 19, last paragraph). Thus, limitations in instant claim 22 are disclosed in the reference. Also, the limitations of instant claims 25, 26, 49, 52, and 53 are taught by Coffee et al. (page 4, second paragraph and third paragraph).

At the time the invention was made, it would have been obvious to have used the polymer fibre scaffold disclosed in Coffee et al. as the polymer serving for cell attachment of the Shastri invention. One of ordinary skill in the art would have been motivated to do this since the Coffee polymer fibre scaffold provides biocompatible polymer as required by the Shastri invention. Furthermore, the methods of Coffee et al. provides for formation of fibres, thus allowing for formation of pores. As pointed out in Shastri et al, a matrix for implantation to form new tissue should be pliable, non-toxic, porous template for vascular ingrowth, wherein the pores should allow vascular ingrowth and the seeding of cells (page 15, lines 13-18). Furthermore, it would have been obvious that the attachment, movement, growth, proliferation, and differentiation would have been altered of any type of cells, including human adherent cells, human fibroblast cells, and stem cells. Thus, the cell types recited in claims 11-14, 16, and 18 (and the preamble of parent claims 1, 14, 16, 18, 20, and 24) are rendered obvious. Additionally, it would have been obvious to have used different types of polylactide, including those recited in instant claim 10, since Coffee et al. broadly teaches the use of polylactide. There would have been a reasonable expectation of success in substituting one polylactide for another.

The references differ from the claimed invention in that they do not expressly disclose selecting a fibre diameter and a size of the gaps between the fibre portions that facilitate a cell process.

Sussman et al. discloses a fibrous matrix for attachment of cells (abstract). For adequate porosity for cell entrance, entrance of nutrients, and for removal of waste products from the fibrous matrix, the pores have a particular diameter and are prepared by using fibers having diameters ranging from about 0.5 to 20 microns (column 4, lines 55-66).

Leong et al. discloses a biodegradable foam scaffold for cell transplantation featuring a continuous network of pores (abstract). Leong et al. points out that "...the vascularization and nature of tissue ingrowth depend on the pore diameter and interconnecting structure" (column 3, lines 43-45). Cells seeded onto the biodegradable foam scaffold generally range from about 7-15 microns in diameter, and include a variety of cells types, including fibroblasts (column 5, lines 24-29).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have varied the gap distance between the fibres in the Coffee scaffold to other gap distances, including those recited in the instant claims, through routine experimentation. Furthermore, one of ordinary skill in the art would have been motivated to do this since Sussman et al. and Leong et al. demonstrate that the gap size affects cell entrance, entrance of nutrients, removal of waste products, vascularization, and nature of tissue ingrowth. Also, it would have been obvious to have used fibre diameters included in the range recited in Sussman et al., which meet the fibre diameter limitation in instant claim 6, since it would have resulted in fibrous matrix pore sizes suitable for cell entrance, entrance of nutrients, and removal of waste products. Given that vascularization and the nature of tissue ingrowth is affected by the pore and fibre diameter sizes, the cell processes recited in the instant claims are facilitated. Furthermore, it would have been obvious to have used cells of the sizes recited in Leong et al. since such cells are suitable for seeding in scaffolds, resulting in vascularization and tissue ingrowth. Thus, claims 2-6, 8, and 9 are also rendered obvious, as well as the gap sizes recited in the parent claims.

A holding of obviousness is clearly required.

Claims 1-16, 18-20, 22, 24-30, 35, 36, and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shastri et al., Coffee et al., Sussman et al., and Leong et al. as applied to claims 1-16, 18, 20, 22, 24-28, 35, 36, and 49-53 above, and further in view of Smith et al. (WO 01/27365) and Simpson et al. (WO 02/40242).

As discussed above, Shastri et al., Coffee et al., Sussman et al., and Leong et al. render claims 1-16, 18, 20, 22, 24-28, 35, 36 and 49-53 obvious. However, these references do not expressly disclose that the polymer used is polycaprolactone.

Smith et al. discloses that polycaprolactone is a polymer suitable for making fiber wherein a polymer solution in a liquid jet is introduced into an electric field and formed and elongated on a surface, such as a wound (page 11, lines 4-6, page 14, lines 17-20, and page 17, lines 14-20).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have created the fibre scaffold rendered obvious by the references with a solution comprising polycaprolactone. One of ordinary skill in the art would have been motivated to do this since polycaprolactone is a polymer which can form fibres on a surface when exposed to an electric field. Thus, limitations recited in claim 19 are rendered obvious by the references.

Additionally, the references differ from the claimed invention in that they do not teach preparing a liquid formulation comprising cell culture medium with a water soluble polymer, or that this liquid formulation is exposed to an electric field to cause the liquid to break into droplets or to form at least one fibre.

Simpson et al. discloses using mixed solutions (nonbiological but biologically compatible material along with substances such as cells) in electroprocessing, wherein fibres or droplets are formed composed of electroprocessed materials as well as one or more substances (page 33, lines 25-28). Electroprocessing is streaming, spraying, sputtering or dripping material across an electric field and toward a target (page 6, lines 37-40).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have introduced mammalian cells by combining a cell culture with a polymer for the formation of fibres by electroprocessing when conducting the invention rendered obvious by the references. One of ordinary skill in the art would have been motivated to do this since this technique is appropriate for delivering cells to an electroprocessed polymer and further would allow formation of fibres as required by Coffee et al. Thus, claims 29 and 30 are rendered obvious.

Note further that Simpson et al. provides further motivation for applying mammalian cells to the fibre scaffold rendered obvious by the references as Simpson et al. teaches combining cells with an electroprocessed collagen matrix in order to provide scaffolding or seeding for the formation of engineered tissue, where the cells include stems cells and fibroblasts (page 17, lines 19-32 and abstract).

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed January 29, 2009, have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features

of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Specifically, the applicant argues that the polymer scaffolds of the claimed invention are not charged or electrically conductive as in the Shastri invention. However, the instant claims do not recite this. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Though the Shastri and Coffee references do not expressly disclose selecting a fiber diameter and a size of the gaps between the fiber portions that facilitate a cell process, the teachings of Sussman et al. and Leong et al. would have motivated the person of ordinary skill in the art to have varied the fiber diameters and gap distances in order to effect cell entrance, entrance of nutrients, removal of waste products, vascularization, and nature of tissue ingrowth. While Sussman does not teach the same polymers as used by the applicant and is directed to the use of a 3-D non-woven fabric matrix used in cell culture of anchorage dependent cells, Sussman is used soley to teach suitable fibre diameters. Further still, given that Sussman teaches the claimed fibre diameters, the ratio of the cell diameter to the diameters of the fibres in the matrix recited in the instant claims are inherently rendered obvious as well. The applicant also asserts that given that Sussman is concerned with growing cells in culture and not with the production of implantable polymer scaffold, it would not be obvious to one skilled in the art to use the fiber diameters included in the range of Sussman. However, an implantable polymer scaffold can be considering a culture for growing cells.

Though Leong et al. does not teach the criticality of the polymer fiber diameter, it is noted that Leong et al. is provided solely to teach the criticality of the pore size of a scaffold and

its teachings are relevant even though Leong et al. teaches a foam scaffold. While Leong et al. teaches cells grown in pores of a foam scaffold rather than a polymer foam, it shows the importance of selecting an appropriate pore size.

Although Coffee et al. does not specifically teach that the polymers are electrically conductive, such types of polymers are not excluded by the Coffee reference. Further still, the polymers can be electret polymers which can be considered electrically conductive. Therefore, the teachings of Coffee et al. may be suitably applied to the teachings of Sastri et al.

With respect to Smith, it is noted that the reference is used solely to render obvious the use of polycaprolactone, and not the teachings regarding nanofibers. With respect to Simpson, it is also noted that it is used solely for its teachings that electroprocessing may be used to expose a liquid formulation to an electric field to cause the liquid to break into droplets or to form at least one fibre.

Therefore, the rejections of record must be maintained.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN E. FERNANDEZ whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
Art Unit 1651

sef